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June 9, 2004

Michael O. Leavitt, Administrator
U.S. Environmental Protection Agency
Ariel Rios Building, 1101-A
1200 Pennsylvania Ave., N.W.
Washington, DC 20460

Subject: Comments on the HPV Test Plan for Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester

Dear Administrator Leavitt:

The following comments on Akzo Nobel's test plan for the chemical Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester are submitted on behalf of the Physicians Committee for Responsible Medicine (PCRM), People for the Ethical Treatment of Animals (PETA), the Humane Society of the United States (HSUS), the Doris Day Animal League, and Earth Island Institute. These health, animal protection, and environmental organizations have a combined membership of more than ten million Americans.

Akzo Nobel Functional Chemicals LLC submitted its test plan on February 10, 2004, for the chemical Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester (CAS No. 2781-11-5). This compound, also referred to as Fyrol 6, is used as a flame retardant for urethane and electronic laminate resin systems, reacting with and becoming a part of the resin system. The sponsor was able to compile existing data on this chemical for most of the SIDS endpoints in the HPV program.

At this time, however, we question Akzo Nobel's assessment that a combined reproductive/developmental toxicity study (OECD 421) is needed to meet the requirements of the HPV program. If conducted, this test will result in the death of at least 675 animals.

After reviewing this test plan, we examined the HPV test plan for a similar chemical, Dimethyl methylphosphonate (CAS No. 756-79-6), sponsored by the DMMP Consortium, which includes Akzo Nobel. Public comments for DMMP are due on July 6, 2004. It appears as though the structures for Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester and for DMMP are similar; although the chemical sponsored in this plan does contain a bis (2-hydroxyethyl) amino side chain. We would like to know if Akzo Nobel has considered placing these two chemicals into a single category. Specifically, all mammalian toxicity endpoints for DMMP have been previously carried out and data from these studies may be used in a weight-of-evidence

approach to satisfy the reproductive and developmental toxicity endpoints of Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester.

We also noted that both Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester and DMMP are used as flame retardants. Also, the trade names of the two chemicals are similar: Fyrol 6 and Fyrol DMMP, respectively. It appears that these two chemicals could be grouped together based on similar physicochemical properties. We would appreciate a description from the sponsor(s) as to how these two chemicals are structurally and functionally related. If the toxicity of both chemicals is similar, a read-across approach using data from DMMP could be used to fill the reproductive and developmental toxicity endpoints for Phosphonic acid, [[bis(2-hydroxyethyl) amino] methyl]-, diethyl ester. This approach is not only a scientifically valid analysis of a chemical's toxicity and adequate for a screening level program, it is also consistent with EPA's stated goal of maximizing the use of existing data in order to limit additional animal testing.

If Akzo Nobel insists on conducting further animal tests on this chemical (OECD 421), we request that the *in vitro* rodent embryonic stem cell test (EST) be conducted in parallel. Although conducting these tests in parallel will not spare any animals at this point in time, it would assist with building the database for this non-animal method for predicting embryotoxicity. The EST has recently become commercially available in the U.S., and was validated by the European Centre for the Validation of Alternative Methods last year. The Centre's Scientific Advisory Committee concluded that the EST was ready to be considered for regulatory purposes (Genschow 2002). This would be a good opportunity for Akzo Nobel to work with EPA and the animal welfare community to incorporate this validated non-animal test into the HPV program.

Thank you for your attention to these comments. I may be reached at 202-686-2210, ext. 327, or via e-mail at *meven@pcrm.org*.

Sincerely,

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Research Analyst

Chad B. Sandusky, Ph.D.
Director of Research

References

Genschow, E., *et al.*, "The ECVAM international validation study on *in vitro* embryotoxicity tests: Results of the definitive phase and evaluation of prediction models", *Alternatives to Laboratory Animals* 30: 151-76, 2002.